Use of a molecular genetic platform technology to produce human wnt proteins reveals distinct local and distal signaling abilities.

Journal: PLoS One

Publication Year: 2013

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PubMed link: 23516471

Funding Grants: WNT signaling and the control of cell fate decisions in human pluripotent stem cells., Interdisciplinary Stem Cell Training Program at UCSD II

Public Summary:
This manuscript describes a novel cell culture system to produce biologically active proteins, such as WNTs, which have potent stem cell activities. The system allows high levels of production of these proteins and will make them more readily available to the scientific community. The papers also elucidate important differences in activities amongst the various WNT proteins, with some acting at long distances and others acting at short distances. The transgenic cell lines will make the use and application of WNT proteins more commonplace and affordable.

Scientific Abstract:
Functional and mechanistic studies of Wnt signaling have been severely hindered by the inaccessibility of bioactive proteins. To overcome this long-standing barrier, we engineered and characterized a panel of Chinese hamster ovary (CHO) cell lines with inducible transgenes encoding tagged and un-tagged human WNT1, WNT3A, WNT5A, WNT7A, WNT11, WNT16 or the soluble Wnt antagonist Fzd8CRD, all integrated into an identical genomic locus. Using a quantitative real-time bioluminescence assay, we show that cells expressing WNT1, 3A and 7A stimulate Wnt/beta-catenin reporter activity, while the other WNT expressing cell lines interfere with this activation. Additionally, in contrast to WNT3A, WNT1 only exhibits activity when cell-associated, and thus only signals to neighboring cells. The reporter assay also revealed a rapid decline of Wnt activity at 37 degrees C, indicating that Wnt activity is highly labile. These engineered cell lines will reduce the cost of making and purifying Wnt proteins and serve as a continuous, reliable and regulatable source of Wnts to research laboratories around the world.